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Innovation and the Burden of Disease: Retrospective Observational Study of New and Emerging Health Technologies Reported by the EuroScan Network from 2000 to 2009

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ABSTRACT

Objectives: Medical innovation in developed countries has been linked to burden of disease, with more innovation in areas representing greater investment return. This study used horizon scanning or early awareness and alert activity as a novel measure of innovation to determine whether new and emerging health technologies reported by international horizon scanning agencies reflected diseases constituting the greatest burden. **Methods:** This was a retrospective observational study of the 20 member agencies of EuroScan (the International Information Network on New and Emerging Health Technologies), representing 17 developed countries. Burden of disease was defined as disability-adjusted life-years, taken from the 2004 World Health Organization Global Burden of Disease estimates. This analysis focused on 102 specific diseases within 21 broader groups. Horizon scanning output was measured as the number of technologies reported by EuroScan member agencies between 2000 and 2009. **Results:** At best there was a weak association between innovation and burden of disease. An apparent high-level association was dependent on just three high-prevalence disease groups: malignant neoplasms, neuropsychiatric conditions, and cardiovascular disease. Disaggregating broader groups into specific diseases further weakened the association. Innovation is disproportionately strong in cancer and nonischemic heart disease and disproportionately weak in mental health. **Conclusions:** Innovations reported by early awareness and alert systems do not always reflect conditions accounting for the highest morbidity and mortality. The results do not support previous reports of a positive relationship between burden of disease and innovation, but accord with evidence of notable discrepancies among key groups. Factors other than disease burden drive innovation.

Keywords: burden of illness, epidemiology, health services, innovation.

Introduction

In developed countries the main disease burden is from noncommunicable conditions, most notably cardiovascular disease, cancer, and neuropsychiatric conditions [1,2]. The development of new health technologies might be expected to focus on diseases with high morbidity and mortality, to reflect areas of greater burden. However, because the innovation process is long, costly [3,4], often unsuccessful, and largely commercially driven, innovation typically reflects all the factors influencing investment return, of which burden of disease is just one [5–7].

The existing evidence of a positive relationship between burden of disease and innovation is based mainly on input measures of innovation such as public and charitable research and development (R&D) funding [8,9]. This association may be a reflection of health-care policy, in particular calls to address the burden of specific diseases including cancer and dementia [10–13]. There are concerns, however, that some disease areas are underfunded. A recent report by the UK Clinical Research Collaboration found that although research spending in the United Kingdom broadly corresponded to burden of disease, cancer attracted a disproportionately high level of funding whereas blood system disorders, cardiovascular diseases, and stroke received comparatively little funding [9]. Furthermore, separating neuropsychiatric conditions into neurological and mental health conditions revealed disproportionately low funding in mental health compared with the related disease burden [14]. This corroborates concerns over a lack of investment in dementia research and services [15–17]. Only Lichtenberg [18] used output measures of innovation and found a positive relationship among developed countries. This was based primarily on pharmaceuticals launched; drugs currently on sale and relevant published articles were used as innovation outcomes in additional analyses, but these were limited to the United States and cancer, respectively.

Horizon scanning or early awareness and alert systems have been implemented in many developed countries to identify new and emerging health technologies, with the aim of managing their introduction into resource-limited health-care systems. One facet of their work is to anticipate technologies that will have a significant, positive impact on patients and systems, and those with

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Table 1 – Reported technologies, DALYs, and deaths for level 1 categories.

Level 1 group	Reported technologies, n(%)	DALYs ('000s)	Deaths ('000s)
I: Communicable, maternal, perinatal, and nutritional conditions	102 (6.9)	2346 (4.6)	196 (5.0)
II: Noncommunicable diseases	1367 (92.4)	45,051 (88.1)	3460 (89.9)
III: Injuries	10 (0.7)	3712 (7.3)	191 (5.0)
Total	*1479 (100)*	*51,109 (100)*	*3847 (100)*

DALYs, disability-adjusted life-years.

potentially negative impacts. The results of horizon scanning activity may be considered an ideal proxy measure for innovation, because it attempts to capture all important new interventions and products relevant to health-care services. This study examines the relationship between disease burden and the reporting of health innovations among the 20 member agencies of EuroScan (the International Information Network on New and Emerging Health Technologies) [19]. We compare health technologies reported by EuroScan from 2000 to 2009 with burden of disease (World Health Organization [WHO]: WHO 2004 estimates) [2] in the 17 developed countries represented, at different levels of disaggregation.

Methods

Innovation: Horizon scanning output

Horizon scanning output was measured as the number of unique technologies uploaded onto the EuroScan database between 2000 and 2009, both inclusive. EuroScan member agencies are all noncommercial, nonprofit organizations operating in relation to regional or national government, representing the following countries: Australia, Austria, Canada, Denmark, England, Finland, France, Germany, Ireland, Israel, Italy, the Netherlands, New Zealand, Norway, Spain (incorporating autonomous regional early awareness and alert systems in Andalucía and the Basque Country), Sweden, and Switzerland (see http://www.euroscan.org.uk). Technologies include drugs, devices, diagnostics, interventions (e.g., surgery), programs (e.g., screening programs), and organizational changes to the delivery of health care (e.g., delivery in different settings) [19].

Burden of disease

Burden of disease was measured as disability-adjusted life-years (DALYs) and deaths for 2004 for countries within EuroScan (updated WHO Global Burden of Disease estimates) [2]. The 2004 estimates were the most up-to-date available. These were summed to generate composite DALYs and deaths for countries represented within EuroScan. Bivariate Pearson's correlations were performed to determine the extent to which DALYs for specific diseases (N = 102; see "Classification of Diseases" section below) were correlated between countries. This was repeated for deaths. A high degree of linear association between all countries for both DALYs and deaths indicated similar distributions of disease burden (DALYs: $r \geq 0.8$, N = 102, $P < 0.001$; deaths: $r \geq 0.8$, N = 102, $P < 0.001$ for all comparisons).

Classification of diseases

Diseases (or causes) are grouped in the first three levels of the four-stage hierarchy used in the WHO Global Burden of Disease studies [1,2]. At the first level, there are three main categories: communicable, maternal, perinatal, and nutritional conditions; noncommunicable diseases; and injuries. At the second level, these categories are broken down into 21 disease groups; for example, "noncommunicable diseases" consists of 14 groups, including malignant neoplasms and diabetes mellitus. At the third level, some of these groups are broken down further into specific diseases; for example, "malignant neoplasms" consists of 17 specific types of cancer. This level also includes "other" categories (e.g., "other malignant neoplasms" includes less common forms of cancer, such as sarcoma and glioma). There are 102 specific diseases at the third level. We created an additional third-level category for "all malignant neoplasms" to take into account technologies that covered multiple types of cancer or were nonspecific. This category is included within the broader "malignant neoplasms" group for analysis at the second level, but not otherwise at the third level.

Assigning disease classification to reported technologies

Of all the technologies uploaded onto the EuroScan database between 2000 and 2009, 45% were drugs, 23% devices, 14% procedures, 12% diagnostics, 3% programs, and <1% settings. The remainder were unspecified. We assigned disease classification codes to technologies in stages. At the first stage, we assigned codes to all entries with an indication clearly specified within the title (e.g., "vaccine for herpes zoster"). Approximately 70% of technologies were coded in this way. At the second stage, we scrutinized the full database records for entries without a clear indication in the title and extracted the information where possible. Technologies that could not be coded included those with vague or very broad indications (e.g., "cancer"), those with no specific indication, and those whose indications could not be linked to specific diseases (e.g., contraception, smoking cessation, and general wound care). Coding did not discriminate between different stages of the same disease; for example, a drug for metastatic melanoma indicated for both stages III and IV disease would be coded only once as melanoma. Technologies with more than one indication received separate codes for each disease.

Statistical analysis

The association between horizon scanning output and burden of disease (DALYs and deaths) was analyzed by using bivariate Pearson's correlations in SPSS Statistics 17.0 (IBM, New York, USA). Fisher's z transformation was used to calculate 95% confidence intervals for each value of r. The analysis was repeated for both broader disease groups (level 2) and specific diseases (level 3).

Results

Of 1451 unique technologies entered on the EuroScan database between 2000 and 2009, 80 (5.5%) could not be coded and were therefore excluded from the analysis. This left 1371 unique technologies with 1479 individual indications. At the first level, noncommunicable diseases accounted for approximately 90% of technologies, DALYs, and deaths (Table 1).

At the second level, three disease groups predominated (Fig. 1). Neuropsychiatric conditions had the most DALYs but dispropor-

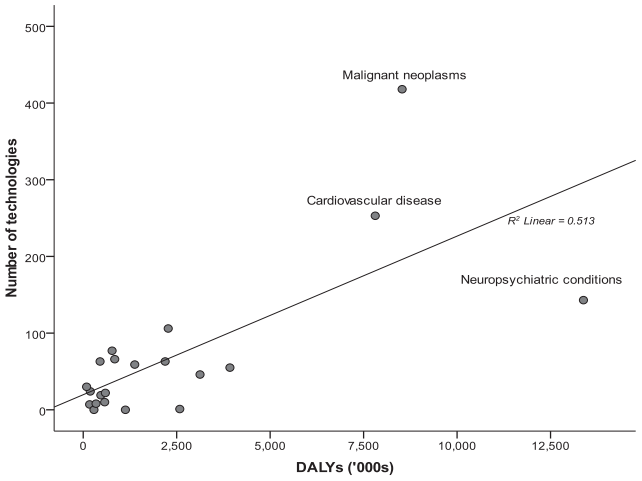

Fig. 1 – Correlation between DALYs and technologies for level 2 disease groups. DALYs, disability-adjusted life-years.

tionately fewer technologies, and malignant neoplasms had the highest number of technologies but disproportionately fewer DALYs. Cardiovascular disease accounted for high numbers of both DALYs and technologies. There was a moderate positive correlation between DALYs and reported technologies ($r = 0.72$, n = 21, $P < 0.001$, 95% CI 0.42–0.88), but this was principally due to the outlier effect of the three key groups. Excluding malignant neoplasms, neuropsychiatric conditions, and cardiovascular disease from the analysis greatly weakened the association among the remaining disease groups ($r = 0.37$, n = 18, $P > 0.05$, 95% CI −0.12 to 0.72). At the third level of disease disaggregation, the association between DALYs and technologies was weaker (Fig. 2; $r = 0.48$, N = 102, $P < 0.001$, 95% CI 0.31–0.62) than at the second level. Diseases within malignant neoplasms consistently had a greater number of technologies than expected based on DALYs, with "other" malignant neoplasms and breast cancer having the greatest discrepancies. Diseases within neuropsychiatric conditions generally had lower technology numbers than expected, with the exception of "other" neuropsychiatric conditions. Diseases within cardiovascular disease were more widely scattered, with "other" cardiovascular diseases representing a disproportionately high number of technologies. Using mortality rather than DALYs did not greatly alter the results, either at the second level of classification ($r = 0.84$, n = 21, $P < 0.001$, 95% CI 0.64–0.93) or at the third level ($r = 0.60$, N = 102, $P < 0.01$, 95% CI 0.45–0.71).

Highest-ranking causes for reported technologies with corresponding DALY and death rankings are shown in Table 2. Of the 30 diseases accounting for the highest numbers of reported technologies, 13 were among the leading DALY causes and 14 among the leading death causes. "Other" cardiovascular diseases had the highest number of technologies, followed by "other" malignant neoplasms. Unipolar depressive disorder had the highest number of DALYs and a relatively low number of technologies. Ischemic heart disease represented the highest number of deaths and was the second highest ranking DALY cause, but had proportionately fewer technologies.

Discussion

Overall we have found at best a weak level of association between innovation and burden of disease. Although the results for a high level of disease aggregation suggest an association, it is dependent on three high-prevalence disease groups: cancers, neuropsychiatric conditions, and cardiovascular disease. The results do not sup-

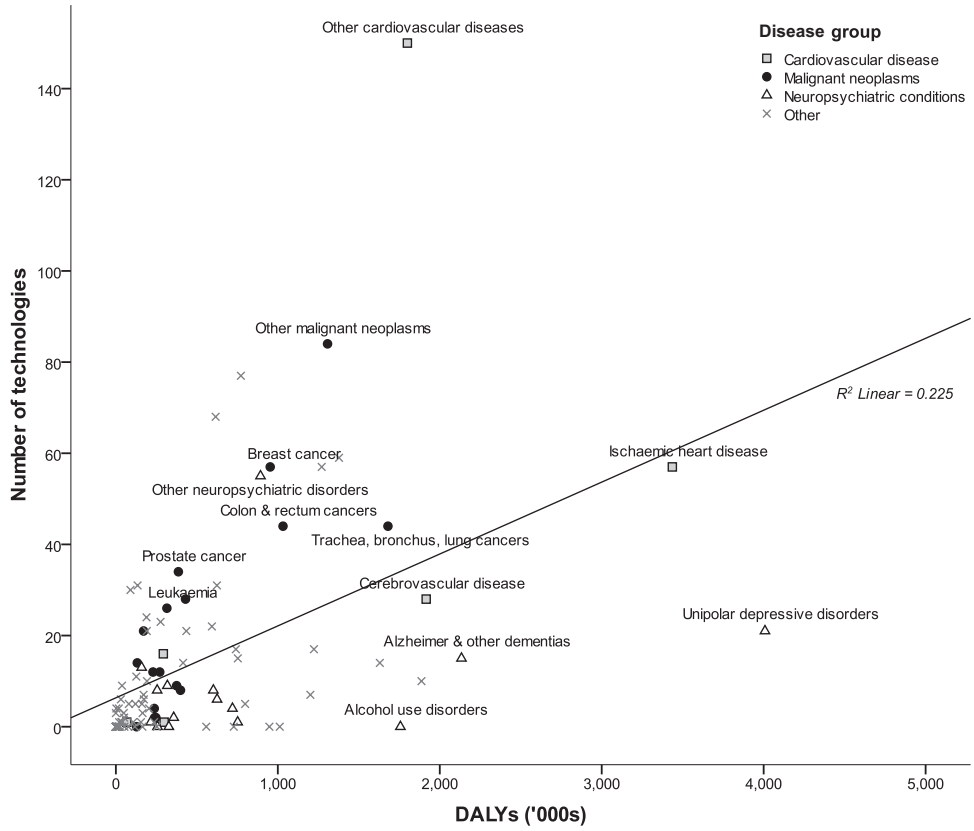

Fig. 2 – Correlation between DALYs and technologies for level 3 causes. DALYs, disability-adjusted life-years.

Table 2 – Highest ranking causes for reported technologies (level 3), with associated DALY and death rankings.

Technologies	Number of technologies	Rank	DALYs ('000s)	Rank	Deaths ('000s)	Rank
Other cardiovascular diseases	150	1	1800	6	386.4	2
Other malignant neoplasms	84	2	1307	11	141.9	5
Endocrine disorders	77	3	772	21	31.6	32
Other musculoskeletal disorders	68	4	616	29	17.4	39
Diabetes mellitus	59	5	1378	10	101.4	11
Breast cancer	57	6	953	17	91.6	12
Ischemic heart disease	57	6	3436	2	644.4	1
Other digestive diseases	57	6	1271	12	109.0	10
Other neuropsychiatric disorders	55	9	893	19	32.1	31
Colon and rectum cancers	44	10	1032	15	140.3	6
Trachea, bronchus, lung cancers	44	10	1680	8	214.4	4
Prostate cancer	34	12	386	37	70.8	13
Macular degeneration and other sense organ diseases	31	13	624	28	0.1	80
Other genitourinary system diseases	31	13	134	68	21.8	37
Skin diseases	30	15	90	75	8.3	47
Lymphomas, multiple myeloma	28	16	430	34	58.7	16
Cerebrovascular disease	28	16	1916	4	357.1	3
Leukemia	26	18	315	42	39.4	24
Other neoplasms	24	19	189	59	33.6	28
Other infectious diseases	23	20	276	45	33.3	30
Congenital anomalies	22	21	593	31	12.1	42
Melanoma and other skin cancers	21	22	171	62	18.7	38
Unipolar depressive disorders	21	22	4008	1	2.0	66
Nephritis and nephrosis	21	22	191	58	46.1	21
Rheumatoid arthritis	21	22	435	33	3.8	60
Asthma	17	26	741	24	8.6	46
Osteoarthritis	17	26	1223	13	1.7	67
Hypertensive heart disease	16	28	293	44	68.4	15
Alzheimer and other dementias	15	29	2134	3	134.4	7
Other respiratory diseases	15	29	753	22	69.7	14

DALYs, disability-adjusted life-years.

port previous reports of a positive relationship between burden of disease and innovation [18] but are consistent with evidence of notable discrepancies among key disease groups [9]. Our results are based on existing horizon scanning systems and so cannot be generalized to developing countries, most of which do not have such systems in place. Others, however, have reported a weaker innovation (and R&D) association with need in developing countries [6–8,18,20,21].

Although our findings are at some odds with previous reports, our study has a number of advantages, albeit with caveats. This is the first study to use horizon scanning output to measure innovation in addressing burden of disease. Unlike research using funding as an indicator of innovation [8,9], we use a measure of output rather than intention to address burden of disease. The data come from 10 years of scanning by an international network of horizon scanning systems. The caveat is that there is heterogeneity between agencies in practice and activity levels [22,23]. Although most agencies cover all diseases, differences in policy and practice mean that the technologies they report may not represent these areas equally, and although arguably the differences balance out it must nevertheless be acknowledged that early awareness and alert activity is an imperfect proxy for innovation. It does not represent all innovations, but only those that have reached a relatively advanced stage of development and are important to the health-care systems supporting this activity. Precision of reporting also varies between agencies: for example, one might report a drug's indication as metastatic breast cancer, whereas another might simply state "breast cancer," although this is not a concern here as the WHO data were grouped only as finely as individual diseases, and not their different types or stages. The WHO DALY methodology is widely accepted, and our DALY association findings are supported by our findings for mortality data alone [2]. One concern with using DALYs for international comparisons is whether the disability weights assigned to each disease have cross-national stability; however, research across developed countries has supported the assumption of universality [24–27].

While disease classification can be problematic, we have deliberately explored its effect. On the one hand, the coarseness of the classification can contribute to the instability of the association; on the other hand, there is a level of disaggregation where a correlation with the relative rarity of innovation would be impossible, but we do not think that that is an issue with the levels of aggregation that we have explored.

To an extent the results accord the current health service and patient emphasis on cancer. Yet they are also consistent with concerns that neuropsychiatric conditions, particularly dementia, are underfunded [15–17]. Dementia has been identified as an R&D priority [11,12], and our findings imply that this is not happening, or at least not leading to final outputs. Two comments are worth noting: first, factors other than absolute disease burden drive innovation. Relatively little is still known about the causes of physiological changes leading to dementia [28], and so the development of disease-modifying therapies will be slower than for conditions where the disease pathophysiology is better established. The high number of cancer technologies suggests an increase in industry breakthroughs in a prominent market. Moreover, the number of new technologies is not necessarily representative of the degree of innovation; for example, one blockbuster drug may have a greater impact on treatment outcomes than do several modifications of existing therapies. Sec-

ondly, the focus of activity among EuroScan agencies tends to be tangible innovations, that is, drugs, devices, and diagnostics rather than programs and prevention, which may be more appropriate for treating and managing neuropsychiatric conditions. The fact that the agencies introducing the vast majority of technologies focus predominantly on drugs [23], which make up a large number of cancer therapies, may also contribute to the high number of technologies in this area. A final issue is whether the burden of disease as measured by DALYs best reflects the need for innovation. While DALYs incorporate both disease severity and the numbers affected, they may not mirror a societal preference for giving priority to some rare conditions. But that is a different issue from that addressed in this article.

Finally, it is important to take context into account when evaluating investment decisions relating to R&D in health care. The relative paucity of tangible innovation does not necessarily mean a reduced focus of concern in low innovation areas. However, the question of how that concern be addressed in the absence of innovation, whether by stimulating innovation or by compensating for its absence in other ways, is wide open.

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